T. Moge

16 17

Attorney Docket No.: 6225.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Koch et al

Serial No.: 10/016,858 Group Art Unit: 1617

Filed: December 14, 2001 Examiner: Hui, San Ming R.

For: Hormone Composition

CERTIFICATE OF MAILING UNDER 37 CFR 1.8(a)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I hereby certify that the attached correspondence comprising:

1. Response
2. Tab 1: Declaration under 37 C.F.R. 1.132 with Exhibit A
3. Curriculum Vitae
4. Tab 2: Reference - Santen et al., Menopause, Vol. 9, No. 3, 2002

is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

On February 25, 2004

Dolly Kapadia
(name of person mailing paper)

Dolly Kapadia
(signature of person mailing paper)

Attorney Docket No.: 6225.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Koch et al

Serial No.: 10/016,858 Group Art Unit: 1617

Filed: December 14, 2001 Examiner: Hui, San Ming R.

For: Hormone Composition

RESPONSE

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed November 25, 2003, kindly consider the following remarks.

Claims 35, 36, 40, 43, 45-47, and 49-53 are pending and at issue.

Claims 35, 36, 40, 43, 45-47, and 49-53 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Mettler et al., in view of Meignant (US Patent No. 6,060,077), in view of Mettler et al., *Maturitas* 14:23, 1991 and Vagifem® monograph (Novo Nordisk® 2000). The Examiner contends that Meignant discloses that use of low doses of estradiol for treating atrophic vaginits; that Mettler et al. disclose vaginal administration of estradiol using tablets; that the Vagifem® monograph discloses tablets containing hypromellose and PEG in their coating; and that it would have been obvious to combine the teachings of these citations to achieve the presently-claimed invention. This rejection is respectfully traversed.

Applicants have previously argued that Meignant does not disclose or suggest a low-dose treatment *regimen* as in the present invention and, to the contrary, teaches away from the present invention by asserting that soft capsules are superior to tablets for vaginal administration of estradiol. It is also Applicants' position that the documented use of Vagifem® per se as described in Mettler et al. (i.e., 25 μg tablets twice weekly) could not have led one of ordinary skill in the art to a reasonable expectation of achieving the benefits of the present invention by using a significantly lower dose of estradiol in a vaginal tablet.

The Examiner's attention is directed to the Declaration Under 37 C.F.R. 1.132 of Dr. Lila E. Nachtigall (hereinafter, "Nachtigall Declaration" attached herewith at Tab 1). Dr. Nachtigall is an internationally recognized expert in the field of hormone replacement therapy who also maintains an extensive clinical practice and thus is well-positioned to evaluate the beliefs of those of ordinary skill in the HRT art at the time the present application was filed.

Dr. Nachtigall states that, in her opinion, nothing in the prior art – or in the clinical experience of HRT medical practitioners – would have suggested that once- or twice-weekly vaginal administration of a tablet containing 10 μg estradiol would be useful to treat atrophic vaginitis (Nachtigall Declaration, at ¶ 3.) Dr. Nachtigall also points out specifically that (i) Meignant does not provide any basis for asserting a clinical benefit for low-dose estradiol administration via a tablet (Nachtigall Declaration at ¶ 4); (ii) Meignant's assertion of superiority for soft capsules over tablets is misplaced (Nachtigall Declaration at ¶ 5); and (iii) even the positive experience of medical practitioners with the present Vagifem® product (25 μg estradiol) would not have supported a reasonable expectation of success with lower doses of estradiol as presently claimed (Nachtigall Declaration at ¶ 6).

The Examiner's attention is also directed to an article entitled "Treatment of urogenital atrophy with low-dose estradiol: preliminary results", by Santen et al., *Menopause* 9:179, 2002 (attached herwith at Tab 2.) This article (which is not prior art against the present claims), reports the results of a study in which a vaginal cream containing 10 μg estradiol/dose was administered daily

for 3 weeks, followed by twice-weekly for an extended period. Notably, the article states: "The lowest dose of vaginal E2 reported to be effective for treating vaginal atrophy is 5-10 μg/*day*, delivered via a silastic ring. The next lowest effective dose is a *daily* 10-μg vaginal tablet." (Santen et al., p 180, first column, last paragraph, emphasis added.) Thus, even after the present invention, there was no recognition by practitioners in the field that a lower dose of estradiol administered via a tablet could be effective in treating atrophic vaginitis.

On this basis, it is respectfully submitted that the presently claimed invention is non-obvious over the cited references and that this rejection should be withdrawn.

It is believed that the claims are in condition for allowance, and a determination to that effect is earnestly solicited.

Respectfully submitted,

Date: February 25, 2004

Reza Green, Reg. No. 38,475
Novo Nordisk Pharmaceuticals, Inc.
100 College Road West
Princeton, NJ 08540
(609) 987-5800

23650
PATENT TRADEMARK OFFICE